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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,659	04/14/2006	Muthiah Manoharan	A2038-7021US	4641

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EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT	PAPER NUMBER
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1635

NOTIFICATION DATE	DELIVERY MODE
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06/27/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gengelso@ll-a.com
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Office Action Summary	Application No.	Applicant(s)	
	10/553,659	MANOHARAN, MUTHIAH	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,18-24 and 41-60 is/are pending in the application.
- 4a) Of the above claim(s) 1,18-24,41-45 and 58-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 46-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/29/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group 2, claims 46-57, in the reply filed on April 4, 2008 is acknowledged.

Claims 1, 18-24, 41-45 and 58-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 4, 2008. It is noted that applicants state these claims are canceled; however, no claim amendment has been submitted and these claims remain pending.

Drawings

The drawings are objected to because due to a dark background part of figure 6 is illegible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an

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application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 46-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Acevedo et al. (US 5,519,134) in view of Scaringe et al. (WO 96/41809, cited on IDS) and Reed et al. (WO 92/03464).

The claims are directed to protected monomers having the formula shown in claim 46, comprising a point of attachment for a ligand or tethered ligand and three points of attachment for first and second functionalized hydroxyl groups and a third protected or unprotected hydroxyl. Specific embodiments define the functionalized hydroxyl groups, the tether and the ligand.

Acevedo et al. teach pyrrolidine monomers suitable for incorporation at any position of a nucleic acid oligomer. The structure of the monomer is shown at column 4 and teaches that the nitrogen atom comprises moiety Q-Z. Q and Z are defined as including linkers containing alkyl, alkenyl or alkynyl chains up to 20 carbon atoms long and terminating in a variety of heteroatom containing functional groups. Acevedo et al.

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further teach at column 4 that in preferred embodiments Z includes fluorenylmethyl, phenyl and benzyl, which are recognized by those in the art as commonly used heteroatom protecting groups that allow additional functionalization after removal.

While Acevedo et al. teach the inclusion of linkers terminating in functional groups at the nitrogen atom of a pyrrolidine monomer, he does not explicitly teach inclusion of a ligand at this position. Acevedo et al. teach synthesis of these monomers as phosphoramidites, but do not teach the use of silyl protecting groups at a primary hydroxyl.

Reed et al. teach the use of pyrrolidine groups as a linker to attach low molecular groups such as cholesterol to an oligonucleotide. The pyrrolidine linkers are illustrated at page 8 and show the conjugate attached through the nitrogen atom.

Scaringe et al. teach protecting groups for nucleic acid synthesis which provide for improved yield. One of these is a silyl protecting groups placed at the 5' (primary hydroxyl) position of the nucleotide sugar, which is shown in figure 1 as it would appear on ribose.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the pyrrolidine monomers taught by Acevedo et al. as suitable for incorporation through chemical oligonucleotide synthesis using the silyl protecting groups taught by Scaringe et al. Based on the teaching of Scaringe et al. that silyl protecting groups are useful in nucleotide synthesis and provide improved yield, one of ordinary skill in the art would recognize use of this protecting group to be a matter of simple substitution of one known element for another that would predictably

provide a monomer that can be incorporated into an oligomer through automated nucleic acid synthesis.

It would further have been obvious and predictable to attach a conjugate group through the nitrogen atom of the pyrrolidine monomer because Acevedo et al. teach the inclusion of alkyl linkers containing heteroatom functional groups at this position which the person of ordinary skill in the art would immediately recognize as a possible point of attachment of a ligand and because Reed et al. actually attach ligands through this position. One of ordinary skill in the art would recognize the production of a tethered ligand wherein the tether has the structure shown in claim 57 to be a matter of design choice made in the course of routine optimization in order to produce a monomer having the best combination of properties for a desired application.

Thus, the invention of claims 46-57 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

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contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Primary Examiner
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